**Site visit inspection report on compliance with HTA licensing standards**

**St James's University Hospital**

**HTA licensing number 12352**

**Licensed under the Human Tissue Act 2004 for the**

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

**27 – 29 June 2017**

**Summary of inspection findings**

The HTA found the Designated Individual (DI), the Licence Holder (LH), the premises and the practices to be suitable in accordance with the requirements of the legislation.

St James's University Hospital (the establishment) was found to have met all HTA standards.

The HTA has given the DI advice with regards to consent, documentation, audit, traceability and temperature monitoring.

Particular examples of good practice are included in the concluding comments section of the report.

**The HTA's regulatory requirements**

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. They are grouped under four headings:

- consent
- governance and quality systems
- traceability
- premises facilities and equipment.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is provided.

HTA inspection reports are published on the HTA's website.

## Background to the establishment and description of inspection activities undertaken

The establishment has been licensed by the HTA since September 2007 and this was the second routine site-visit inspection to assess whether it continues to meet the HTA's standards. The timetable for the site visit was developed taking into account the establishment's latest self-assessed compliance information, a review of the previous inspection findings and pre-inspection discussions with the DI. During the site visit, a visual inspection of the premises including all areas where human tissue was stored, a review of documentation, round table discussions with establishment staff who manage the various tissue collections, as well as a number of audits, were undertaken.

The establishment includes licensed premises at St James's University Hospital, the hub premises, and two satellite premises, located at Chapel Allerton Hospital and the University of Leeds. The majority of the tissue collections stored under the licence are held within ethically approved research tissue banks (RTBs). The establishment also has some collections of tissues which are being stored appropriately under the establishment's licence but are not held as part of an RTB. In total, there are eight distinct collections of tissue being held under the establishment's licence.

The RTBs storing tissues under the establishment's licence include a Multidisciplinary RTB, NIHR RTB, Breast Tissue RTB, paroxysmal nocturnal hemoglobinuria (PNH) RTB and a Dental RTB. In addition, other tissue collections include a selection of tissues collected as part of clinical trials which originally were stored outside of the establishment's licence under recognised research ethical committee approval. The tissues collected as part of the clinical trials have consent for their continued storage for use in further unspecified research. As the ethical approval for these tissue collections has expired the tissues are now appropriately stored under the establishment's licence. There are also two collections of tissues stored at the university satellite site. One collection represents various different types of tissues which are used in multiple academic research projects. A second collection of tissues is also stored under the licence and relate to research associated with 'the ageing aorta'.

During the inspection, each of the above groups operating under the authority of the establishment's licence was visited. The visits all included an orientation meeting where establishment staff could inform the inspection team about the samples that are being stored, the source of the samples and if/how samples are released for use in research. Following the orientation meeting, a visual inspection of the storage facility where each of the groups stored their samples was undertaken. As part of this exercise, a traceability audit was undertaken and where possible, signed donor consent forms relating to the samples were sought. If a group stores tissue under more than one storage condition for example, -80$^{o}$C storage, formalin fixed paraffin-embedded tissue (FFPE) blocks and liquid nitrogen storage, areas covering each type of storage were visited. During the various visual inspections, the inspection team also discussed security, monitoring of the storage facilities and any alarm systems used by the establishment to alert them to any deviations from the required storage conditions. Finally, a round table discussion was held with each group during which consent forms and donor information leaflets were reviewed. Additionally during the round table discussions, each group was asked to talk through their audit activity, incident reporting, risk assessments and other governance systems.

The DI has set up a matrix structure under the licence, lead by herself, and in which each group storing tissue under the licence has nominated a Person Designated (PD). The PDs act as links between the licensable activity and the DI. The DI holds governance meetings, which are used to discuss current projects such as the changes being made to the establishment's sample traceability database. The traceability database is used by all research groups storing tissue except two which have their own bespoke databases. Although governance meetings are themed, the DI reports that, at the end of each meeting,

there is an ‘any other business’ section where any other licensable activity matters can be raised and discussed. In addition to these governance meetings, the DI attends ‘HTA management meetings’ and ‘Research Sub Group’ meetings. The HTA management meetings are chaired by the Hospital Trust’s Director of Quality and include DIs from all of the Trust’s HTA licences. The Research Sub Group meeting is chaired by the University’s Head of Research and Innovation Support and is also attended by the team who are responsible for the administration of the establishment’s traceability database.

The DI has written core procedures which research groups acting under the licence can use. These include seeking consent, document control, staff training, adverse events, complaints, transportation and disposal. In addition to these core documents, each group has created their own bespoke procedures which describe individual procedures specific to that group.

As described above, during the visual inspection a traceability audit of tissue for each group storing tissue under the licence was undertaken.

Some groups hold original copies of donor consent forms. Other groups do not have access to these forms as samples were collected elsewhere as part of a larger study or by different research teams. In these cases, the group assured itself that appropriate consent has been obtained by reviewing the consent information and consent forms used in the studies and from assurances by collaborators that only consented donor samples had been sent for storage. Finally, for samples such as tissue remaining following diagnostic analysis or where samples have been taken directly from the hospital Trust’s patients as part of a study, the individual donor consent form was held securely in a Trust database. During the audits undertaken within the various groups storing tissue, consent documentation relating to the samples chosen as part of the audit was sought and reviewed where possible.

A summary table of samples selected for audit from each group can be found below.

| | Storage type | | | | | | |
|---|---|---|---|---|---|---|---|
| | -80°C | Liquid Nitrogen | FFPE | Slide | -30°C | -150oC | Room temp |
| NIHR | 4 | | | | | | |
| Multidisciplinary | 11 | 3 | 9 | 1 | | | |
| Breast RTB | 6 | | 7 | | | | |
| Chapel Allerton | 4 | | | | 4 | 1 | |
| University | 3 | | | | | 1 | |
| Ageing Aorta | 47 | | | | | | |
| PNH | 4 | | | | | | |
| Dental | | | | | | | 5 |

The identification on each sample was used to review the details held in the establishment’s traceability databases. The locations recorded in the databases were cross-checked with the actual locations of the samples. In addition, and where possible, consent documentation relating to these samples was also sought. In summary, no anomalies were found during the audit, in either the sample location databases or with the associated donor consent forms.

**Inspection findings**

The HTA found the Licence Holder, the Designated Individual and the premises to be suitable in accordance with the requirements of the legislation.

## Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

## Advice

The HTA advises the DI to consider the following to further improve practices:

| No. | Standard | Advice |
|---|---|---|
| 1. | C1(a) | Dental Group<br>During consent seeking discussions with potential donors of teeth, the dental group discuss the possibility of the teeth being stored and used in the same areas as animal teeth. Discussions with establishment staff could not identify the source of this information and it was unclear if indeed any animal tissue was used in the group's laboratories. The DI is advised to work with the establishment's researchers to clarify whether the donated teeth are stored or used in the same areas as animal teeth in order to inform the discussions held when seeking consent from potential teeth donors. |
| 2. | C1(a) | Licence Wide<br>The DI is advised to review the establishment's donor withdrawal procedures to ensure that donors of tissue are clear about the best person or group to contact if they wish to withdraw their consent to the continued retention and use of their tissue. The DI may wish to consider using a generic contact number for each group's office, rather than a specific individual, as this may help minimise the risk of a donor not being able to contact the individual who may have ceased working at the establishment or is otherwise unavailable. |
| 3. | C1(d) | Dental Group<br>A review of the donor information leaflet used by the dental collection group highlighted some text which could be interpreted in different ways. Establishment staff understand this text to indicate that any living cells cultured from the pulp of the donated teeth would only be kept for a maximum period of ten years. This statement however could be interpreted as indicating that donated teeth will be kept for a maximum period of ten years following their donation.<br>The DI is advised to review the donor information sheet in collaboration with the group's researchers with the aim of clarifying the text so that the intended retention period of the donated teeth is clear to those giving consent and donating their teeth for research. The DI may also wish to seek advice from the appropriate research ethics committee on their interpretation of the ambiguous text. |
| 4. | C1(d) | Chapel Allerton<br>The group at Chapel Allerton have identified a discrepancy between the consent form and the participant information sheet used in a study during which blood and tissue biopsies were collected. The participant information sheet includes details of this continued storage of blood and biopsies taken as part of the clinical study and the establishment staff reported that patients had been made aware when consenting that both blood and tissue biopsies would be taken and stored as part of the research project; however, the consent form references only the retention of the blood samples. Although this does not mean that donors of samples were not fully informed about the storage of the biopsy samples when they were giving their consent, the donor consent form |

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|---|---|---|
| | | does not explicitly record the donor's consent for the storage of the biopsy samples. The group has identified this discrepancy and wish to ensure that study participant's consent to the continued storage of the biopsies is appropriately recorded on a consent form and intend to re-confirm the participant's consent by asking participants to sign a new form or indicate that they no longer wish to have samples retained.<br><br>The DI may wish to liaise with the research ethics committee that granted approval for the original study in case the committee has any additional guidance with regards to contacting the study participants for their further consent. |
| 5. | GQ1(b) | Ageing Aorta<br><br>The group has also recently drafted several SOPs however, these are not version controlled. The DI is advised to ensure that the group's SOPs are contained within an appropriate governance system so that they are version controlled and staff therefore can assure themselves that they are accessing the most recent version. |
| 6. | GQ2(a) | Chapel Allerton<br><br>The Chapel Allerton group collect samples as part of various clinical trials. During the conduct of the trial, samples that have been collected are recorded onto the group's dedicated tracking database and added to appropriate sample storage boxes within the 'on-going collection' freezer. The sample storage boxes are audited by establishment staff when full and as they are placed into their long term storage freezer location. These audits confirm that the location of each sample has been correctly recorded on the group's tracking database.<br><br>The DI is advised to consider performing interim audits of these 'on-going' sample collection boxes so that any discrepancies between the samples and the tracking database can be detected at an early stage. This may be useful as sample boxes from studies that are slow to recruit participants may take longer to become full and therefore any errors would potentially not be identified for some time, meaning investigating subsequent discrepancies may be more difficult. |
| 7. | GQ2(a) | Ageing Aorta<br><br>The Ageing Aorta group have recently undertaken a full review of all stored samples and assured themselves that the tracking database accurately reflects the actual samples stored. The collection of samples is currently relatively static with no additional samples being added and only a few post-doctoral researchers associated with the group's research accessing the collection.<br><br>The DI is advised to devise a suitable programme for auditing the sample collection on an on-going basis, taking into account the limited access to the samples and reflecting the recent full audit conducted by the research group. |
| 8. | GQ6(a) | Ageing Aorta<br><br>The Ageing Aorta group have referenced the core risk assessments created by the DI in the group's quality manual which include risks such as equipment failure. However, the establishment has no risk assessments relating specifically to the sample collection. The DI is advised to review any risks posed to the samples and document any risks not contained within the core documents in a group specific risk assessment. In addition, the DI is advised that if the group re-commences collecting samples or supplying samples to other researchers in the future, then specific risk assessments covering these new activities will be required. |

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| 9. | T1(a) | Breast RTB<br><br>An audit of samples in the breast RTB, from another organisation, revealed that the prefix of each sample's identification code had been incorrectly recorded in the establishment's sample tracking database. The DI was given advice during the inspection regarding amending the database records to reflect the correct identification code as written on each sample.<br><br>Post inspection update - Prior to the release of the draft inspection report, the DI confirmed that this action has been completed and all relevant sample records have now been updated. |
| 10. | T1(c) | Multidisciplinary RTB<br><br>During the audit of samples held within the multidisciplinary RTB, it was noted that some sample boxes containing sample vials within the freezer were labelled only on the box lid. The DI is advised to ensure that both the lid and the base of the sample box are labelled so that both are identifiable. Having the base of the sample box labelled may help to ensure that the orientation of the box is easily identifiable if a lid is mistakenly placed onto the box in the worng orientation. Labelling the base may also help to reduce the risk of an incorrect lid being placed onto another sample box in error during sample deposition or retrieval activity, which may in turn pose a risk to sample traceability. |
| 11. | PFE2(c) | Licence Wide<br><br>The main freezer store room used by the multidisciplinary, breast and NIHR groups is air-conditioned to mitigate the effect of the heat generated by the large number of -80$^{o}$C freezers within the room. If there was a failure of the air-conditioning unit, the temperature of the room would rise significantly and possibly to a level which could effect the efficient operation of the freezers, posing a potential risk to the stored samples.<br><br>The DI is advised to consider adding a room temperature monitoring probe linked to the same remote monitoring system as the freezers themselves. In the event of a failure of the air-conditioning unit, any subsequent increase of room temperature could be detected early by the room temperature monitor, ideally before the operation of the freezers was affected. |
| 12. | PFE2(c) | Chapel Allerton<br><br>During the audit of samples held at the Chapel Allerton group's storage facility, it was noted that the ambient temperature of the room containing the storage freezers was high. This may pose a risk to the efficient operation of the sample storage freezers. The DI is advised to monitor and keep the temperature of the room under review to assure herself that the operation of the freezers is not compromised by the elevated ambient room temperature. |
| 13. | PFE2(c) | Licence Wide<br><br>The establishment's freezers are monitored and alarm if the temperature deviates from the expected range. If alarming establishment staff are alerted via either, an automated dial-out system or through a 24-hour monitoring organisation. In the event of an alarm triggering, establishment staff are contacted sequentially using an emergency call-out list.<br><br>The DI is advised to challenge the alarm system during out of hours periods so that the alarm triggers. Challenging the alarm system in this way may help the DI to assure herself that alarm conditions are responded to appropriately by establishment staff on the call-out list. |

## Concluding comments

During the inspection, examples of good practice were observed, which have been included below.

Staff in the NIHR and multidisciplinary RTBs have received training in the use of the establishment's liquid nitrogen cryostore. This training not only includes procedures for adding and removing samples from the store but also general housekeeping around the use of the storage tanks. These housekeeping procedures include monitoring the temperature prior to opening the tank and ensuring that the storage tank is not open for too long and cleaning ice from the storage racks prior to returning them to the store. This helps to maintain the storage racks and sample boxes in an ice-free condition, which facilitates access to the samples.

The study nurse working on the breast RTB reviews a checklist of topics that must be covered during the seeking of informed consent. The use of this checklist helps to assure the DI that all necessary information has been given to a tissue donor and that the donor has had an opportunity to discuss them during the consent process.

Establishment staff at the university satellite site demonstrated a positive culture towards the reporting of incidents. All incidents, whether minor or major and independent to there being any effect on the stored tissue, were reported and investigated. Consistent reporting of incidents and sharing of the learning from them helps to improve procedures and to identify measures to mitigate against various risks.

The PD in the recently formed PNH group has undertaken significant training of all laboratory staff involved with the human tissue collection. Training given to PDs has been disseminated by the PD to the laboratory staff so that they have a good understanding of the regulatory environment in which they are working. This has helped to increase awareness regarding the requirements of the HT Act.

At a whole establishment level the DI continues to develop new systems to facilitate audit activity within each research group. The DI already requires all research groups working under the licence to undertake regular audits of some of the samples that are in storage. To facilitate this process, new functionality has been added to the database used to track the majority of the samples under the licence. This functionality will select a subset of samples that are being stored by each group and provide these details to the group so that they can be audited. Results of the audit will then be recorded in the database so that they may be reviewed by the DI and other researchers. This functionality will help to maintain oversight of each group's samples and to help assure the DI that traceability information is being appropriately entered and updated.

The HTA has assessed the establishment as suitable to be licensed for the activities specified.

**Report sent to DI for factual accuracy: 27 July 2017**

**Report returned from DI: 14 August 2017**

**Final report issued: 31 August 2017**

## Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

| Consent standards |
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| **C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice** |
| a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.<br>b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.<br>c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.<br>d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.<br>e) Language translations are available when appropriate.<br>f) Information is available in formats appropriate to the situation. |
| **C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent** |
| a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.<br>b) Records demonstrate up-to-date staff training.<br>c) Competency is assessed and maintained. |

| Governance and quality system standards |
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| **GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process** |
| a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.<br>b) There is a document control system.<br>c) There are change control mechanisms for the implementation of new operational procedures.<br>d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.<br>e) There is a system for managing complaints. |
| **GQ2 There is a documented system of audit** |
| a) There is a documented schedule of audits covering licensable activities.<br>b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these. |

| **GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills** |
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| a) Qualifications of staff and all training are recorded, records showing attendance at training. |
| b) There are documented induction training programmes for new staff. |
| c) Training provisions include those for visiting staff. |
| d) Staff have appraisals and personal development plans. |
| **GQ4 There is a systematic and planned approach to the management of records** |
| a) There are suitable systems for the creation, review, amendment, retention and destruction of records. |
| b) There are provisions for back-up / recovery in the event of loss of records. |
| c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing). |
| **GQ5 There are systems to ensure that all adverse events are investigated promptly** |
| a) Staff are instructed in how to use incident reporting systems. |
| b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made. |
| **GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored** |
| a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. |
| b) Risk assessments are reviewed regularly. |
| c) Staff can access risk assessments and are made aware of risks during training. |

| **Traceability standards** |
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| **T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail** |
| a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it. |
| b) A register of donated material, and the associated products where relevant, is maintained. |
| c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom. |
| d) A system is in place to ensure that traceability of relevant material is maintained during transport. |
| e) Records of transportation and delivery are kept. |
| f) Records of any agreements with courier or transport companies are kept. |
| g) Records of any agreements with recipients of relevant material are kept. |

| T2 Bodies and human tissue are disposed of in an appropriate manner |
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| a) Disposal is carried out in accordance with the HTA's Codes of Practice. |
| b) The date, reason for disposal and the method used are documented. |

| Premises, facilities and equipment standards |
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| **PFE1 The premises are secure and fit for purpose** |
| a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. |
| b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained. |
| c) There are documented cleaning and decontamination procedures. |
| **PFE2 There are appropriate facilities for the storage of bodies and human tissue** |
| a) There is sufficient storage capacity. |
| b) Where relevant, storage arrangements ensure the dignity of the deceased. |
| c) Storage conditions are monitored, recorded and acted on when required. |
| d) There are documented contingency plans in place in case of failure in storage area. |
| **PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored** |
| a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept. |
| b) Users have access to instructions for equipment and are aware of how to report an equipment problem. |
| c) Staff are provided with suitable personal protective equipment. |

## Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

   *or*

   A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall that:

   - poses a risk to human safety and/or dignity, or
   - indicates a failure to carry out satisfactory procedures, or
   - indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
   - has the potential to become a critical shortfall unless addressed

   *or*

   A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

   In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

## Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.